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A randomized study of dietary composition during weight-loss maintenance: Rationale, study design, intervention, and assessment

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ABSTRACT

Background: While many people with overweight or obesity can lose weight temporarily, most have difficulty maintaining weight loss over the long term. Studies of dietary composition typically focus on weight loss, rather than weight-loss maintenance, and rely on nutrition education and dietary counseling, rather than controlled feeding protocols. Variation in initial weight loss and insufficient differentiation among treatments confound interpretation of results and compromise conclusions regarding the weight-independent effects of dietary composition. The aim of the present study was to evaluate three test diets differing in carbohydrate-to-fat ratio during weight-loss maintenance.

Design and dietary interventions: Following weight loss corresponding to 12 ± 2% of baseline body weight on a standard run-in diet, 164 participants aged 18 to 65 years were randomly assigned to one of three test diets for weight-loss maintenance through 20 weeks (test phase). We fed them high-carbohydrate (60% of energy from carbohydrate, 20% fat), moderate-carbohydrate (40% carbohydrate, 40% fat), and low-carbohydrate (20% carbohydrate, 60% fat) diets, controlled for protein content (20% of energy). During a 2-week *ad libitum* feeding phase following the test phase, we assessed the effect of the test diets on body weight.

Outcomes: The primary outcome was total energy expenditure, assessed by doubly-labeled water methodology. Secondary outcomes included resting energy expenditure and physical activity, chronic disease risk factors, and variables to inform an understanding of physiological mechanisms by which dietary carbohydrate-to-fat ratio might influence metabolism. Weight change during the *ad libitum* feeding phase was conceptualized as a proxy measure of hunger.

1. Introduction

In the US, about 50% of adults with overweight or obesity are trying to lose weight, often by following energy-restricted diets [1]. While many experience some initial success, most have difficulty maintaining clinically significant weight loss over the long term [2,3]. A common explanation for weight regain relates to behavior, in that motivation to adhere to a dietary prescription typically diminishes with time. Indeed, behavioral intervention trials indicate a direct association between adherence and weight loss, regardless of dietary treatment [4–6]. An alternative explanation relates to biology, in that weight loss elicits adaptations that promote weight regain, including a decline in energy expenditure and an increase in hunger [7,8]. Whether macronutrient composition influences these adaptations remains a subject of debate [9,10].

For most of the last half century, dietary fat restriction was the primary focus of clinical practice guidelines and public health

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recommendations for weight loss and chronic disease risk management. Alternative strategies that focus on modifying carbohydrate amount and paying attention to carbohydrate source (choosing foods with a low glycemic index) have gained attention over the last two decades [11,12]. Lowering dietary glycemic load [13–15] using these strategies may produce beneficial effects on metabolism and hunger compared to conventional low-fat (high-carbohydrate) diets. Acutely, beneficial effects may include hormonal changes that increase availability of metabolic fuels in the late postprandial period (attenuated insulin levels, for example), and thereby decrease hunger and voluntary food intake [16,17]. Chronically, lowering glycemic load appears to lessen the fall in resting and total energy expenditure (TEE) that predictably occurs during weight loss [18–20], although the mechanisms for this effect remain speculative. While some nutrition experts advocate decreasing carbohydrate to reduce dietary glycemic load [21], others contend that substantial benefit can be achieved with a moderate decrease in carbohydrate intake so long as the carbohydrate source has a low glycemic index [22]. Still others argue that clinical care for patients with obesity and general public health messages should remain focused on lowering energy intake, pointing out that fat is an easily over-consumed and energy-dense macronutrient [23].

The primary aim of this study was to evaluate the effect of three diets varying widely in carbohydrate-to-fat ratio (high-carbohydrate, moderate-carbohydrate, low-carbohydrate) on energy expenditure during weight-loss maintenance, using a controlled feeding protocol. The primary outcome was TEE, assessed by doubly-labeled water methodology. Outcomes for additional specific aims are presented in Section 5 of this protocol paper.

2. Study design and infrastructure

The study was a randomized controlled trial (RCT) comprising run-in, test, and *ad libitum* feeding phases (Fig. 1). The purpose of the run-in phase was to obtain baseline measurements and restrict energy intake to achieve a 12 ± 2% decrease in body weight. Participants who were unable to achieve this level of weight loss were dismissed from the study prior to randomization. The purpose of the test phase was to compare the metabolic effects of high-, moderate-, and low- (HI-, MOD-, and LO-) carbohydrate diets during weight-loss maintenance and explore physiological mechanisms underlying these effects. We assessed study outcomes at baseline (BSL), post-weight loss (PWL, time 0), and midpoint (MID, weeks 8–10) and end (END, weeks 18–20) of the test phase. The purpose of the *ad libitum* feeding phase was to evaluate the effects of the test diets on change in body weight, as a proxy measure of hunger.

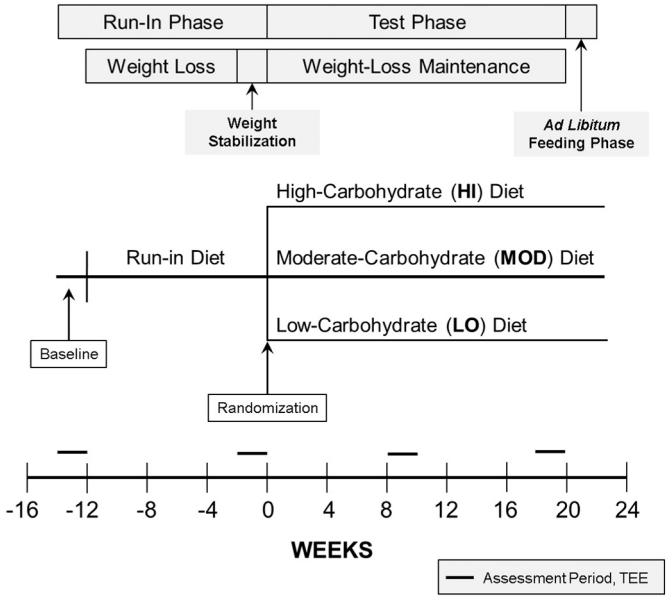

Fig. 1. Study design.

Researchers from Boston Children's Hospital and Harvard Medical School partnered with faculty and staff at Framingham State University (FSU), Sodexo, and Assabet Valley Regional Technical High School (AV). The study was known as the Framingham State Food Study, or (FS)2. We decided against a hospital-based feeding study, recognizing challenges associated with recruiting participants willing and able to travel to a research center in the city on a daily basis, limited space in research kitchens, inability to provide freshly prepared meals three times per day, and cost. Rather, we formed a novel collaboration with FSU, located about 20 miles west of Boston, and Sodexo, the food service contractor at FSU. We had access to ample on-site facilities including large and well-equipped commercial kitchens, a dining area where participants ate supervised meals, and on-campus space that was transformed into a research center for conducting assessments. We established a satellite feeding site at AV, located about 10 miles north of Framingham, to expand our catchment area and meet recruitment goals. Collaborating with the school nutrition program at AV, we had access to a commercial kitchen and dining space. We hired a contractor to build kiosks for preparing and serving study foods adjacent to dining areas in both locations (FSU and AV).

All study protocols were approved by the Institutional Review Board at Boston Children's Hospital. We obtained written informed consent prior to baseline assessments. The stipend for full study participation was $3280, and study meals and snacks were valued at $3220, for total compensation of $6500. The study was conducted between August 2014 and May 2017.

The leadership team included two principal investigators, two study directors (one from BCH to oversee all day-to-day operations, another from FSU to serve as a liaison with BCH regarding study infrastructure), an associate study director, a nutrition research manager, a Sodexo director of dining services, a biostatistician, and a data and quality manager. This team stayed in close communication with executive staff at FSU (e.g., vice president of academic affairs and provost, executive vice president) and AV (*e.g.,* superintendent-director, director of business operations). Study staff included employees with varying levels of effort from BCH (study physician, support dietitian, diet technician, statistical programmer, research assistants and study coordinators), FSU (financial coordinator, faculty and staff who volunteered on study work groups), Sodexo (program manager/lead dietitian, staff dietitian, chefs), and AV (food service director, head chef, sous chef). We also hired *per diem* nurses, radiology technologists, and research assistants to help with study visits, meal preparation (*e.g.,* weighing and serving foods), and data entry. Most of the research assistants were students at FSU.

3. Participants

3.1. Eligibility criteria

We enrolled faculty, staff, students, and residents of communities surrounding FSU and AV who met the eligibility criteria listed in Table 1. We specified BMI ≥ 25 kg/m^2, which corresponds to the conventional definition of overweight, as an inclusion criterion but did not enroll anybody who weighed > 350 lbs. (159 kg), to avoid exceeding upper weight limits for some assessment equipment. We excluded anyone who reported recent and substantial weight change or behaviors that could confound study outcomes (adherence to a special diet or vigorous-intensity physical activity regimen, use of medications or dietary supplements, smoking, excessive alcohol consumption). We excluded those who had abnormal results from screening laboratory tests, indicative of unrecognized illness. We did not enroll individuals who had vacation plans which precluded shipment of food (*e.g.,*